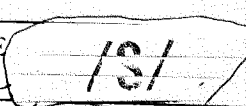


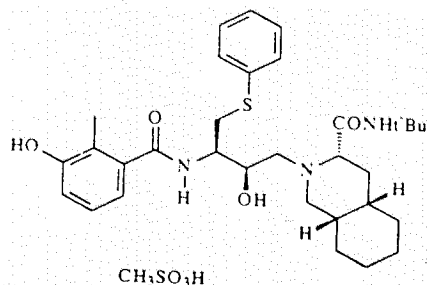
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER for: 020779, S022

PHARMACOLOGY REVIEW(S)

BEST POSSIBLE COPY

SUPPLEMENTAL NDA CHEMIST'S REVIEW		1. ORGANIZATION HFD-530		2. NDA NUMBER 20-779	
3. NAME AND ADDRESS OF APPLICANT (City and State) Agouron Pharmaceuticals, Inc. 10350 North Torrey Pines Road La Jolla, CA 92037-1022				4. AF NUMBER	
				5. SUPPLEMENT(S)	
				NUMBER(S) SE2-022	DATE(S) 1/26/99
6. NAME OF DRUG VIRACEPT [®] Tablets		7. NONPROPRIETARY NAME nelfinavir mesylate tablets			
8. SUPPLEMENT(S) PROVIDES FOR: BID dosing of Viracept (nelfinavir mesylate) tablets.				9. AMENDMENTS / REPORTS Amendment of 11/22/99	
10. PHARMACOLOGICAL CATEGORY Anti-HIV		11. HOW DISPENSED <input checked="" type="checkbox"/> Rx <input type="checkbox"/> OTC		12. RELATED IND/NDA/DMF(S)	
13. DOSAGE FORM(S) Tablets		14. POTENCY(IES) 250 mg			
15. CHEMICAL NAME AND STRUCTURE [3S-[2(2S*,3S*,3 α ,4 α β ,8 α β)]-N-(1,1-dimethylethyl)decahydro-2-[2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino-4-(phenylthio)butyl]-3-isoquinolinecarboxamide], monomethanesulfonate (salt)				16. MEMORANDA	
17. COMMENTS None					
18. CONCLUSIONS AND RECOMMENDATIONS This Supplement provides for BID dosing of Viracept (nelfinavir mesylate) tablets. All CMC information has been previously submitted and approved. The package insert notes that the bottles now contain 300 tablets (as discussed during the review of 20-779/SCS-023), the tablets are film coated (reviewed in 20-779/SCF-027), the container should be kept tightly closed, and the tablets should be dispensed in the original container. In addition, the container label now contains the statements "Keep container tightly closed" and "Dispense in original container". This Supplement is therefore recommended for approval from a CMC perspective.					
19. REVIEWER					
NAME George Lunn, Ph.D.		SIGNATURE 		DATE COMPLETED 1/24/99	
20. CONCURRENCE: HFD-530/SMiller					
DISTRIBUTION	<input checked="" type="checkbox"/> Original Jacket	<input checked="" type="checkbox"/> GLunn	<input checked="" type="checkbox"/> SLynche		
	<input checked="" type="checkbox"/> Division File	<input checked="" type="checkbox"/> SMiller	<input checked="" type="checkbox"/> Med		
	<input checked="" type="checkbox"/> HFD-830/CChen	<input checked="" type="checkbox"/> Micro	<input checked="" type="checkbox"/> PharmTox		



REVIEW AND EVALUATION OF PHARMACOLOGY/TOXICOLOGY DATA

KEY WORDS:

REVIEWER NAME:

DIVISION NAME:

HFD#:

REVIEW COMPLETION DATE:

ELECTRONIC FILE NUMBER:

NDA NUMBERS:

SERIAL #/DATE/TYPE OF SUBMISSION:

INFORMATION TO SPONSOR:

SPONSOR (OR AGENT):

MANUFACTURER OF DRUG SUBSTANCE:

Ita Yuen

Division of Antiviral Drug Products

530

11/5/99

None

20,778 (Oral powder) & 20,779 (Tablets)

022/January 26, 1999/Efficacy & labeling
supplement

Yes () No (X)

Agouron Pharmaceuticals, Inc.

10350 North Torrey Pines Road

La Jolla, CA 92037-1020

DRUG:

Generic Name:

Trade Name:

Nelfinavir mesylate (AG1343)
VIRACEPT®

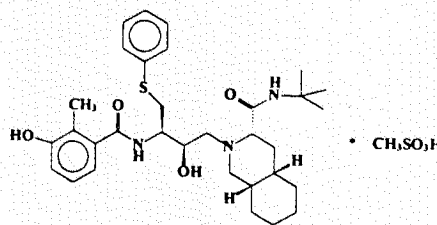
Chemical Name:

[3*S*-[2(2*S**, 3*S**), 3 α , 4 α β , 8 α β]]-*N*-(1,1-dimethylethyl)decahydro-2-[2-hydroxy-3[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-3-isoquinolinecarboxymaide monomethanesulfonate (salt)

CAS Registry Numbers:

159989-65-8 (AG1343)

159989-64-7 (AG1346)

Molecular Formula/Molecular Weight: $C_{32}H_{45}N_3O_4S$ (free base)/M.W. = 567.79 $C_{32}H_{45}N_3O_4S \cdot CH_4O_3S$ (salt)/M.W. = 663.90**Structure:****RELEVANT INDS/NDAS/DMFS:**

IND []

DRUG CLASS:

HIV protease inhibitor

INDICATION:

Treatment of HIV infection

CLINICAL FORMULATION:

VIRACEPT Tablets are supplied as a light blue, capsule-shaped tablet in a 250 mg strength (the weight of free base) containing calcium silicate, crospovidone, magnesium stearate, and FD&C blue #2 powder. VIRACEPT Oral Powder is available in a 50 mg/g strength (the weight of free base) containing microcrystalline cellulose, maltodextrin, dibasic potassium phosphate, crospovidone, hydroxypropyl methylcellulose, aspartame, sucrose palmitate, and natural and artificial flavor.

ROUTE OF ADMINISTRATION:

Oral

PROPOSED CLINICAL USE:

Treatment of HIV infection

INTRODUCTION AND DRUG HISTORY:

Nelfinavir is a protease inhibitor which has demonstrated significant *in vitro* and clinical activity against HIV. Clinical studies have shown the drug to be relative safe, especially compared to previously marketed HIV protease inhibitors. In addition, nelfinavir appears to produce a different pattern of viral resistance compared to other protease inhibitors. Like other drug in this class, nelfinavir is extensively metabolized. VIRACEPT received accelerated